# Peanut oral immunotherapy decreases IgE to Ara h 2 and Ara h 6 but does not enhance sensitization to cross-reactive allergens

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# Peanut oral immunotherapy decreases IgE to Ara h 2 and Ara h 6 but does not enhance sensitization to cross-reactive allergens

*To the Editor:*

Oral immunotherapy (OIT) induces specific $IgG_4$ antibodies and regulatory T cells and leads to suppression of IgE-mediated reactions.[1] In pollen immunotherapy, specific IgE levels to pollen allergens decrease with increasing $IgG_4$.[2,3] We aimed to study whether peanut OIT would induce neosensitization or affect cross-reactive proteins by analyzing IgE sensitization profiles using microarrays. In addition, we analyzed $IgG_4$-IgE ratios to peanut allergens during OIT and assessed whether the cumulative protein dose ingested during treatment determines the changes in $IgG_4$/IgE.

Fifty-eight 6- to 18-year-old children and adolescents having moderate-to-severe peanut allergy participated in the study. The diagnosis was based on a double-blind placebo-controlled peanut challenge (n = 52) or serum IgE to Ara h 2 above 25 kU/L (27.8-365 kU/L) (n = 6). Thirty-nine patients received peanut OIT, whereas 19 patients continued to avoid peanuts. During 8 months, the daily peanut protein intake increased from 0.1 to 800 mg, after which patients ingested 4 peanuts daily. During the first 19 build-up weeks, the patients used roasted defatted peanut flour (Byrd Mill, Ashland, Va), which showed 100% allergen activity of Ara h 1, 2, 3, and 6, 30% of Ara h 8, but lack of (<20%) Ara h 9 activity in Immuno Solid-phase Allergen Chip (ImmunoCAP ISAC, Thermo Fisher Scientific, Uppsala, Sweden) inhibition assay.[4] From week 20 on, the patients consumed whole peanuts. Serum samples were drawn at baseline and after build-up.

We measured serum IgE to 112 allergen components using the ISAC with a detection limit of 0.3 ISAC standardized units for specific IgE (ISU-E). We measured IgE to hazelnut Cor a 14 and cashew Ana o 3, and IgE and $IgG_4$ to whole peanut extract, Ara h 1, 2, 3, 8, and 9, using ImmunoCAP (Thermo Fisher Scientific). IgE and $IgG_4$ to Ara h 6 were measured using an experimental ImmunoCAP test. Sensitization was defined as ≥0.3 ISU-E. The ethics committee at the Helsinki University Hospital approved the study protocol. Patients and 1 of their parents provided informed written consent. Data analysis protocols can be found in the Online Repository (available at www.jacionline.org).

At baseline, all 58 patients were sensitized to Ara h 2 (97%) and/or Ara h 6 (98%). In addition, the majority was sensitized to Ara h 1 (74%), Ara h 3 (70%), or Ara h 8 (79%), but only 9% were sensitized to Ara h 9. Sensitization to any Ara h 8–cross-reactive pathogenesis-related proteins group 10 (PR-10) protein occurred

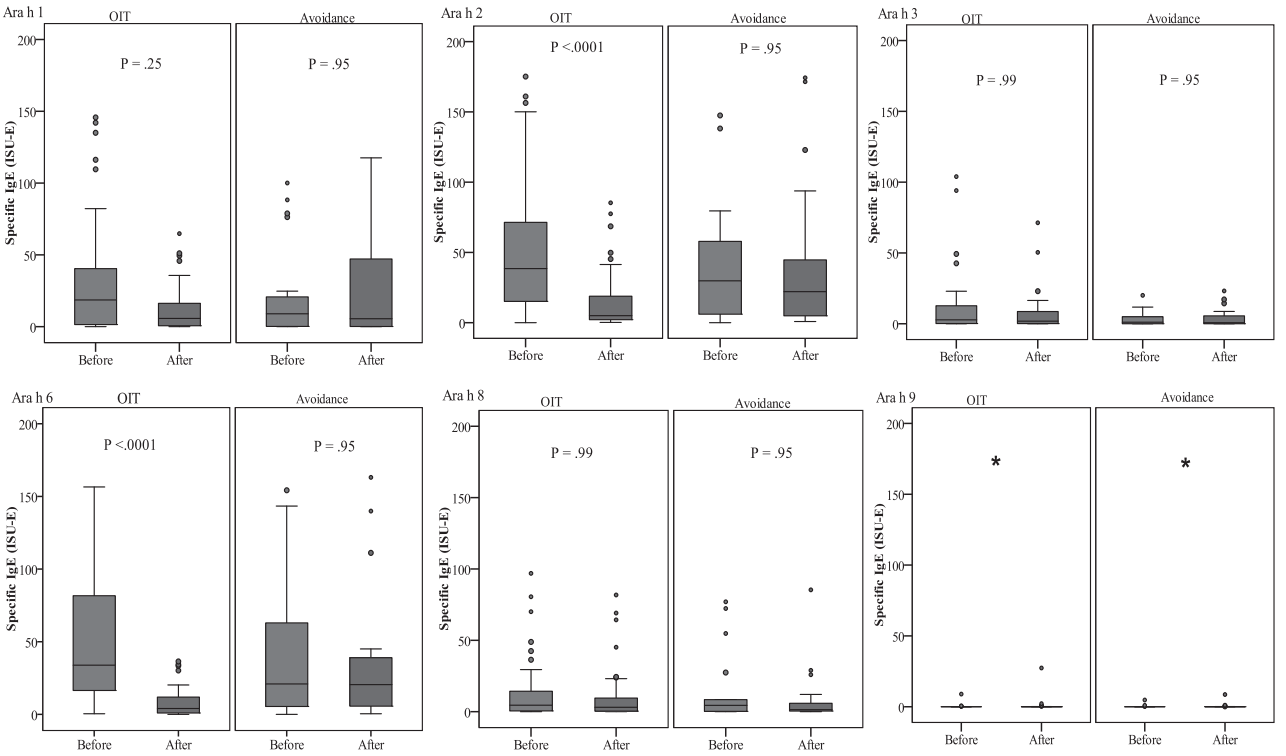


**FIG 1.** Serum peanut allergen-specific IgE measured with ISAC microarray before and after peanut OIT build-up phase. *Omitted from microarray data analysis. Only allergens with ≥50% + 1 patients sensitized (≥0.3 ISU-E) in ≥1of 4 groups (OIT pre, OIT post, avoidance pre, avoidance post) are included in order to ensure the representativeness of the given allergen. See the Methods in this article's Online Repository (available at www.jacionline.org).

in 51 patients (88%) (see Table E1 and Fig E1 in this article's Online Repository at www.jacionline.org).

Of the 39 OIT patients, 34 achieved the maintenance dose and 4 patients discontinued treatment because of side effects and 1 for nonmedical reasons. In the avoidance group, 6 of 19 experienced a single accidental exposure to a peanut or an unknown nut.

Specific IgE to Ara h 2 and 6, which are the best markers of severe peanut allergy,[4] decreased significantly from median 39 ISU-E (range, 1.0-176) to 6 ISU-E (range, 1.2-86) and from 35 ISU-E (range, 1.4-157) to 4.9 ISU-E (range, 1.0-37) ($P < .0001$), respectively, during OIT. No significant changes occurred in specific IgE to Ara h 1, 3, 8, or 9 (Fig 1). The dominance of serological response to Ara h 2 over Ara h 1 and 3 in peanut OIT has been observed in previous studies in children and adolescents.[5,6] OIT did not affect specific IgE to other 2S albumins Ber e 1, Ses i 1, Fag e 2, Jug r 1 (ISAC microarray), Cor a 14, or Ana o 3 (ImmunoCAP) (data not shown). PR-10, lipid transfer protein, and profilin allergen families were unaffected (see Table E2 in this article's Online Repository at www.jacionline.org). Thus, peanut OIT had no effect on specific IgE levels of other 2S albumins, and neosensitization to these allergens did not occur. As specific IgE to hazelnut and cashew 2S albumins were unaffected, the treatment modifies only peanut allergy despite the cosensitization to other nuts. Despite the exposure to Ara h 8 during OIT, our patients showed no changes in the levels of IgE to Ara h 8, Bet v 1, or other PR-10 proteins. This might be because, despite Ara h 8 retaining some activity in roasted products, its amount is small and it is degraded in the gastrointestinal tract. Or, sensitization to Ara h 8 is mainly driven by Bet v 1 and therefore OIT seems not to affect IgE responses to Ara h 8. This is supported by the fact that in contrast to peanut OIT, subcutaneous birch-pollen immunotherapy may decrease IgE to cross-reactive PR-10 proteins.[2]

We observed no neosensitizations to Ara h 9 or other lipid transfer proteins, though Ara h 9 content is low in peanuts[7] as well as it was in roasted peanut flour[4] despite its heat stability.

Specific $IgG_4$ to Ara h 1, 2, 3, 6, 8, 9, and whole peanut extract were low at baseline but increased significantly—except for Ara h 8 and 9—during OIT (see Table E3 and Fig E2 in this article's Online Repository at www.jacionline.org). $IgG_4$-IgE ratios for Ara h 1, 2, 3, 6, and whole peanut extract increased significantly, whereas those for Ara h 8 and 9 remained stable (Fig 2). The increase in $IgG_4$-IgE correlated with the cumulative amount of peanut protein ingested during OIT. The strongest correlations were observed for Ara h 2 (Spearman $\rho = 0.50$, $P = .001$), Ara h 6 ($\rho = 0.36$, $P = .026$) ($n = 38$), Ara h 3 ($\rho = 0.43$, $P = .007$), and whole peanut extract ($\rho = 0.47$, $P = .002$). In sensitized individuals, a high peanut-specific $IgG_4$-IgE ratio predicts tolerance.[8,9] The infrequent sensitization to Ara h 9 at baseline might explain why peanut OIT lacked an effect on the Ara h 9–specific $IgG_4$-IgE ratio, because pretreatment IgE response to a specific allergen seems to be necessary for the induction of $IgG_4$ antibodies by immunotherapy.[3] However, unaffected $IgG_4$-IgE ratio for Ara h 8 cannot be explained by low pretreatment IgE response, as the majority of our patients

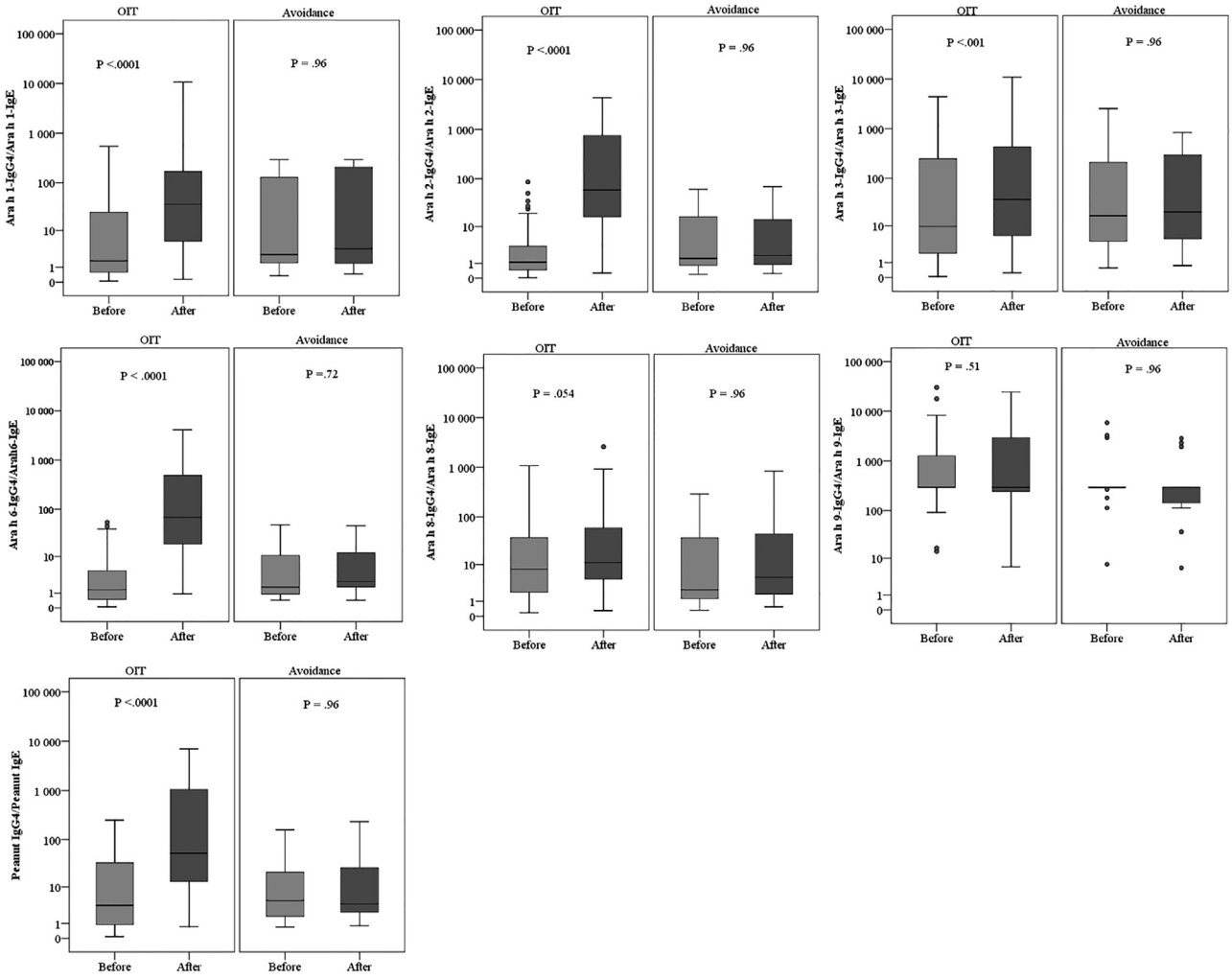


**FIG 2.** $IgG_4$-IgE ratios to peanut allergens and whole peanut extract measured with ImmunoCAP before and after peanut OIT build-up phase.

were sensitized to Ara h 8 at baseline. The specific $IgG_4$-IgE ratio to Ara h 1, 2, 3, 6, and whole peanut extract increased more in patients who ingested larger cumulative allergen dose; thus, the ratio may function as a proxy for success in OIT.

In conclusion, during peanut OIT, the serological response is directed to the peanut storage proteins, and especially, to the 2S albumins. No neosensitization to cross-reactive allergens emerges.

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## Tofacitinib relieves symptoms of stimulator of interferon genes (STING)–associated vasculopathy with onset in infancy caused by 2 *de novo* variants in *TMEM173*

*To the Editor:*

Stimulator of interferon genes (STING), which is encoded by transmembrane protein 173 *(TMEM173)*, is an important mediator in initiating innate immune responses by detecting aberrant DNA species or cyclic di-GMP-AMP (cGAMP) in the cytosol and driving synthesis of type I interferon.[1-3] cGAMP molecules, which are produced by cyclic GMP-AMP synthase, bind to STING homodimers embedded in the endoplasmic reticulum membrane and eventually cause phosphorylation of interferon regulatory factor 3 by activating Tank-binding kinase 1 (TBK1). Patients with activating mutations of STING display early onset of chronic inflammation and vasculopathy caused by increased type I interferon signaling, a condition termed STING-associated vasculopathy with onset in infancy (SAVI).[2,3] Improved understanding of STING's function and its implications in disease pathogenesis has suggested new potential avenues of disease treatment options through modulating STING signaling pathway components.

A 9-year-old Korean boy presented with systemic hyperinflammatory symptoms, including skin lesions, brain infarctions, and pulmonary dysfunction. From 6 months of age, he experienced recurrent infections, including acute otitis media, pneumonia, and gastroenteritis. Telangiectatic skin mottling on both the hands and feet was evident from 12 months of age, which progressed to the extremities and face over time (Fig 1, *A*, and see Fig E1 in this article's Online Repository at www.jacionline.org). At 5 years of age, he was hospitalized because of pneumococcal meningitis, and brain magnetic resonance imaging and magnetic resonance angiography revealed evidence of infarction in the right parietal area. Chest computed tomography at 8 years of age showed evidence of obliterative bronchiolitis with peribronchial inflammation (Fig 1, *B*). Consequently, the patient experienced sudden left leg weakness and headache. Brain magnetic resonance imaging revealed acute infarction in the right anterior watershed area and subarachnoid hemorrhages, and magnetic resonance angiography showed diffuse advanced luminal irregularities throughout the cerebral arteries (Fig 1, *C*). At 9 years of age, a low nasal bridge was apparent and likely caused by a perforated nasal septum (Fig 1, *D*). Generalized telangiectatic rashes on the cheeks, nose, arms, legs, hands, and feet, with gangrenous lesions, were associated with his recurrent infections. He had slight dyspnea, which worsened on physical exertion but needed continuous supplemental oxygen of 1 L/min or more to maintain an oxygen saturation measured by pulse oximetry of between 90% and 95%. Wheezing and crackles were audible in both lower lung fields.

Trio-based whole-exome sequencing was performed (Fig 1, *E*, and see Table E1 in this article's Online Repository at www.jacionline.org) to search for variants that were specifically found in the patient. Among the candidates, 2 *de novo* variants of *TMEM173* appeared to be the most promising based on known disease associations with the patient's phenotype (Fig 1, *F*, and see Table E2 and Figs E2 and E3 in this article's Online Repository at www.jacionline.org). To determine whether the 2 variants occurred in the same chromosome (in *cis*) or on different chromosomes (in *trans*), we amplified a 3.8-kb fragment of *TMEM173* that encompasses both variants, sequenced it using the PacBio sequencing platform, and found that both variants occurred in the paternal chromosome (see Fig E2).

The variants were not observed in any of the public (1000 Genomes and ExAC) or private (1060 healthy Koreans) databases, and the corresponding amino acid residues are strongly conserved among vertebrate orthologs (Fig 1, *G*). The changes were predicted to be damaging by using variant effect prediction software, and the amino acids are located on the transmembrane (p.Ser102Pro) and cytoplasmic domains (p.Phe279Leu), which are involved in homodimerization and are distant from previously reported pathogenic mutations on exon 5 (Fig 1, *H*, and see Tables E2 and E3 in this article's Online Repository at www.jacionline.org). Analysis of the protein structure reveals that Phe279 is located on the N-terminus of the fourth α-helix, which converges physically with the N-terminus of the first α-helix, possibly affecting nearby amino acids, including Asn154 and Val155, which were found to be mutated in patients with SAVI (Fig 1, *I*). Analysis of Ser102 was unavailable, although a recent study suggests that Ser103 is important for maintaining proper subcellular localization.[4]

Based on the known functions of STING, we investigated further the functional consequences of the STING variants. First, patient-derived fibroblasts displayed increased expression of IFN-β, helping to explain the increased inflammatory responses in the patient (Fig 2, *A*). To understand the molecular basis for increased IFN-β expression, we monitored IFN-β promoter activity by expressing the various mutant STING proteins in HEK293T cells (Fig 2, *B*). As the cGAMP concentration increases, cells expressing the mutant STING proteins had increased IFN-β promoter activity compared with cells expressing the wild-type STING but with 2 notable differences from previous observations. First, the double-mutant STING (S102P + F279L) showed stronger activity than the STING with a single mutation (S102P or F279L), implying an additive mode of action by the 2 variants. Second, at a baseline level, the mutant STING proteins barely displayed any IFN-β promoter

# METHODS

## Statistical analysis

We filtered the ISAC microarray data so that the measured value of an allergen had to be above the detection limit (0.3 ISU-E) in ≥50% + 1 of the individuals in ≥1experimental group (OIT group pre, OIT group post, avoidance group pre, or avoidance group post) in order for the allergen to be considered representative and included in the analysis. We fitted a linear model to investigate the effects of treatment, response, subject, sex, age, and season. Furthermore, we used the eBayes test for pairwise comparisons of interest. *P* values were corrected in each pairwise comparison by using the Benjamini-Hochberg procedure.[E1]

For analyses other than that of ISAC microarray data, we used Fisher exact test and the Mann-Whitney *U* test for comparing 2 groups and the Wilcoxon signed rank test for comparing repeated measurements. For the $IgG_4$-IgE ratios, IgE was converted to mg/L with a conversion factor of 1 kU/L = 0.0024 mg/L.[E2]

We used R software, version 3.0 (R Project for Statistical Computing, R Foundation, Vienna, Austria; http://www.r-project.org/) with limma package[E3] and IBM SPSS Statistics 22 (IBM, Armonk, NY).

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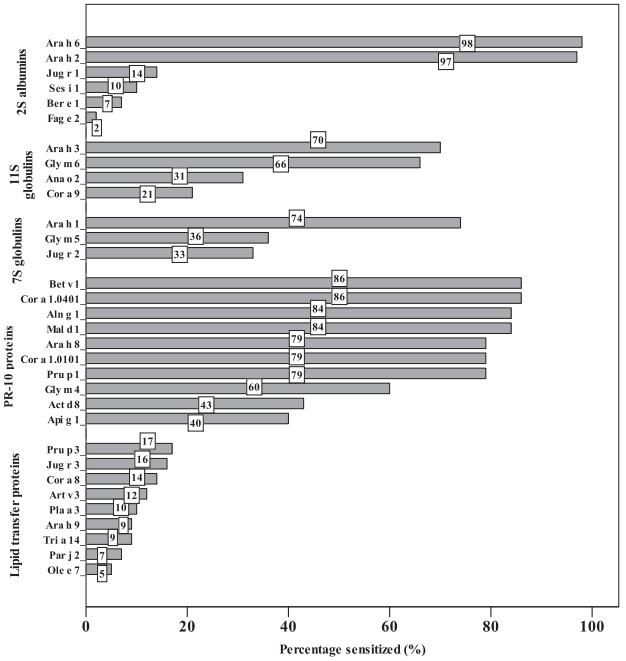


**FIG E1.** Sensitization prevalences (%) to individual allergens in protein families cross-reactive to peanut.

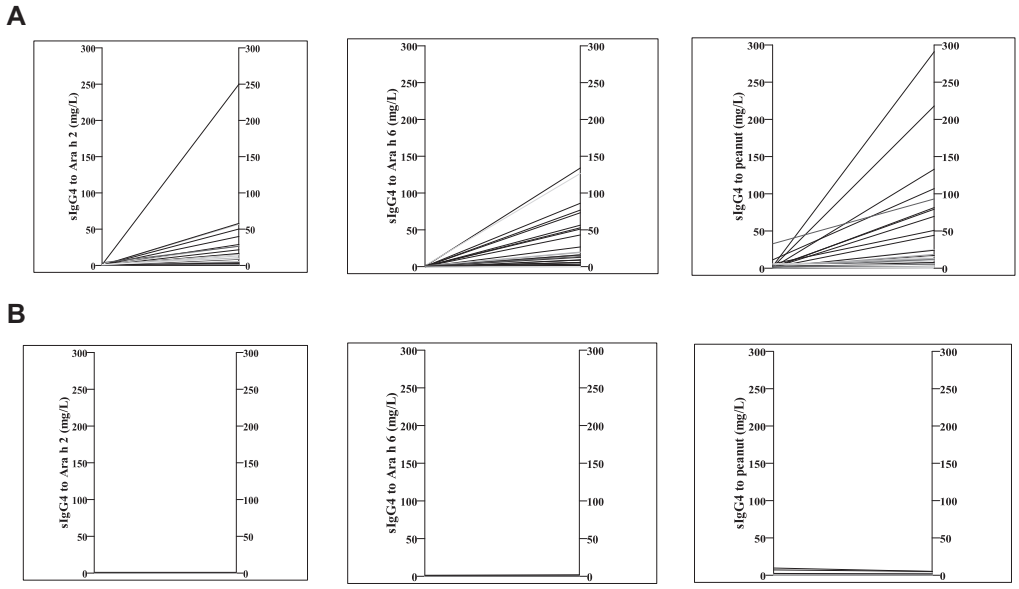


**FIG E2.** Changes in the levels of specific $IgG_4$ to Ara h 2, Ara h 6, and whole peanut extract measured with ImmunoCAP in **(A)** OIT group and **(B)** avoidance group before and after peanut OIT build-up phase.

**TABLE E1.** Baseline characteristics of the patients in the OIT and avoidance groups

| | OIT n= 39 | Avoidance n = 19 | *P* value |
|---|---|---|---|
| Male, n (%) | 22 (56) | 12 (63) | .78 |
| Age (y), median (range) | 8.3 (6.3-18.6) | 8.6 (6.0-13.7) | .97 |
| S-IgE (kU/L), median (range) | 676 (95-4458) | 759 (116-11182) | .46 |
| Time from baseline blood sample to end-of study blood sample (mo), median (range) | 16 (4-28) | 19 (11-31) | .01 |
| Cumulative dose of peanut protein (g), mean (95% CI) | 77 (65-90) | 0 (0) | <.001 |
| Peanut IgE ImmunoCAP (kU/L), median (range) | 75 (1.8-1820) | 66 (0.9-876) | .57 |
| Ara h 2 IgE ImmunoCAP (kU/L), median (range) | 44 (0.6-699) | 32 (1.0-365) | .49 |
| Ara h 6 IgE ImmunoCAP (kU/L), median (range) | 36 (0.3-354)* | 22 (0.8-441) | .78 |

*n = 38.

**TABLE E2.** Specific IgE levels measured with ISAC microarray

| | OIT n = 39 | | | | | | Avoidance n = 19 | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Specific IgE (ISU-E)** | **Pre** | | **Post** | | **Nominal *P* value** | **Adjusted *P* value** | **Pre** | | **Post** | | **Nominal *P* value** | **Adjusted *P* value** |
| 2S albumins | | | | | | | | | | | | |
| Ara h 2 | 39 | 0.3-175 | 5.0 | 0.3-85 | <.0001 | <.0001 | 30 | 0.3-148 | 22 | 0.84-174 | .95 | .95 |
| Ara h 6 | 34 | 0.41-157 | 3.9 | 0.3-36 | <.0001 | <.0001 | 21 | 0.3-154 | 21 | 0.40-163 | .61 | .95 |
| Ber e 1 | 0.3 | 0.3-1.0 | 0.3 | 0.3-2.0 | — | — | 0.3 | 0.3-0.4 | 0.3 | 0.3-1.5 | — | — |
| Fag e 2 | 0.3 | 0.3-0.3 | 0.3 | 0.3-0.3 | — | — | 0.3 | 0.3-0.3 | 0.3 | 0.3-0.3 | — | — |
| Jug r 1 | 0.3 | 0.3-24 | 0.3 | 0.3-62 | — | — | 0.3 | 0.3-86 | 0.3 | 0.3-45 | — | — |
| Ses i 1 | 0.3 | 0.3-3.1 | 0.3 | 0.3-2.5 | — | — | 0.3 | 0.3-2.4 | 0.3 | 0.3-1.7 | — | — |
| 7S globulins | | | | | | | | | | | | |
| Ara h 1 | 19 | 0.3-146 | 5.8 | 0.3-65 | .04 | .25 | 9.0 | 0.3-100 | 5.5 | 0.3-118 | .93 | .95 |
| Gly m 5 | 0.3 | 0.3-26 | 0.3 | 0.3-35 | — | — | 0.3 | 0.3-27 | 0.3 | 0.3-35 | — | — |
| Jug r 2 | 0.3 | 0.3-4.6 | 0.3 | 0.3-6.2 | — | — | 0.3 | 0.3-3.2 | 0.3 | 0.3-2.8 | — | — |
| 11S globulins | | | | | | | | | | | | |
| Ana o 2 | 0.3 | 0.3-6.8 | 0.3 | 0.3-14 | — | — | 0.3 | 0.3-4.2 | 0.3 | 0.3-11 | — | — |
| Ara h 3 | 2.8 | 0.3-104 | 1.8 | 0.3-71 | .33 | .99 | 1.1 | 0.3-20 | 0.7 | 0.3-23 | .80 | .95 |
| Cor a 9 | 0.3 | 0.3-6.8 | 0.3 | 0.3-7.2 | — | — | 0.3 | 0.3-2.3 | 0.3 | 0.3-124 | — | — |
| Gly m 6 | 0.6 | 0.3-51 | 0.6 | 0.3-50 | .85 | .99 | 0.6 | 0.3-12 | 0.5 | 0.3-27 | .76 | .95 |
| LTP | | | | | | | | | | | | |
| Ara h 9 | 0.3 | 0.3-8.9 | 0.3 | 0.3-27 | — | — | 0.3 | 0.3-4.7 | 0.3 | 0.3-8.6 | — | — |
| Art v 3 | 0.3 | 0.3-3.2 | 0.3 | 0.3-5.6 | — | — | 0.3 | 0.3-2.9 | 0.3 | 0.3-3.3 | — | — |
| Cor a 8 | 0.3 | 0.3-1.5 | 0.3 | 0.3-5.4 | — | — | 0.3 | 0.3-0.7 | 0.3 | 0.3-15 | — | — |
| Jug r 3 | 0.3 | 0.3-3.7 | 0.3 | 0.3-7.8 | — | — | 0.3 | 0.3-2.4 | 0.3 | 0.3-4.4 | — | — |
| Ole e 7 | 0.3 | 0.3-1.1 | 0.3 | 0.3-8.8 | — | — | 0.3 | 0.3-1.7 | 0.3 | 0.3-0.3 | — | — |
| Par j 2 | 0.3 | 0.3-1.0 | 0.3 | 0.3-0.4 | — | — | 0.3 | 0.3-2.1 | 0.3 | 0.3-31 | — | — |
| Pla a 3 | 0.3 | 0.3-2.2 | 0.3 | 0.3-6.9 | — | — | 0.3 | 0.3-3.8 | 0.3 | 0.3-5.1 | — | — |
| Pru p 3 | 0.3 | 0.3-2.8 | 0.3 | 0.3-7.0 | — | — | 0.3 | 0.3-2.6 | 0.3 | 0.3-17 | — | — |
| Tri a 14 | 0.3 | 0.3-2.2 | 0.3 | 0.3-1.7 | — | — | 0.3 | 0.3-38 | 0.3 | 0.3-103 | — | — |
| PR-10 | | | | | | | | | | | | |
| Act d 8 | 0.3 | 0.3-13 | 0.3 | 0.3-29 | — | — | 0.3 | 0.3-29 | 0.3 | 0.3-60 | — | — |
| Aln g 1 | 12 | 0.3-158 | 9.4 | 0.3-83 | .60 | .99 | 9.7 | 0.3-140 | 4.6 | 0.3-72 | .31 | .95 |
| Api g 1 | 0.3 | 0.3-22 | 0.3 | 0.3-21 | — | — | 0.3 | 0.3-2.7 | 0.3 | 0.3-30 | — | — |
| Ara h 8 | 4.6 | 0.3-97 | 3.1 | 0.3-82 | .43 | .99 | 4.5 | 0.3-77 | 1.5 | 0.3-85 | .42 | .95 |
| Bet v 1 | 48 | 0.3-163 | 37 | 0.3-162 | .64 | .99 | 56 | 0.3-175 | 46 | 0.3-176 | .67 | .95 |
| Cor a 1.0101 | 4.6 | 0.3-77 | 4.1 | 0.3-50 | .73 | .99 | 2.5 | 0.3-91 | 2.2 | 0.3-79 | .46 | .95 |
| Cor a 1.0401 | 11 | 0.3-128 | 9.1 | 0.3-59 | .99 | .99 | 7.2 | 0.3-112 | 6.8 | 0.3-99 | .80 | .95 |
| Gly m 4 | 0.9 | 0.3-87 | 1.2 | 0.3-62 | .88 | .99 | 0.5 | 0.3-75 | 0.6 | 0.3-38 | .84 | .95 |
| Mal d 1 | 14 | 0.3-157 | 9.7 | 0.3-130 | .58 | .99 | 14 | 0.3-150 | 9.2 | 0.3-160 | .50 | .95 |
| Pru p 1 | 7.9 | 0.3-126 | 7.2 | 0.3-103 | .68 | .99 | 6.9 | 0.3-136 | 2.6 | 0.3-157 | .41 | .95 |
| Profilins | | | | | | | | | | | | |
| Bet v 2 | 0.3 | 0.3-86 | 0.3 | 0.3-22 | — | — | 0.3 | 0.3-52 | 0.3 | 0.3-66 | — | — |
| Hev b 8 | 0.3 | 0.3-121 | 0.3 | 0.3-35 | — | — | 0.3 | 0.3-69 | 0.3 | 0.3-85 | — | — |
| Mer a 1 | 0.3 | 0.3-82 | 0.3 | 0.3-18 | — | — | 0.3 | 0.3-54 | 0.3 | 0.3-90 | — | — |
| Phl p 12 | 0.3 | 0.3-26 | 0.3 | 0.3-7.5 | — | — | 0.3 | 0.3-5.2 | 0.3 | 0.3-22 | — | — |
| Grass group 1 | | | | | | | | | | | | |
| Phl p 1 | 1.6 | 0.3-131 | 1.6 | 0.3-162 | .93 | .99 | 4.4 | 0.3-141 | 5.5 | 0.3-115 | .92 | .95 |

Values are presented as median, range. —, Omitted from microarray data analysis. Only allergens with ≥50% + 1 patients sensitized (≥0.3 ISU-E) in ≥1of 4 groups (OIT pre, OIT post, avoidance pre, avoidance post) are included in order to ensure the representativeness of the given allergen.
*LTP*, Lipid transfer protein.

**TABLE E3.** Changes in levels of specific $IgG_4$ in the OIT and avoidance groups measured with ImmunoCAP

| | OIT n = 39 | | | Avoidance n = 19 | | |
|---|---|---|---|---|---|---|
| **Specific $IgG_4$** | **Baseline** | **Post** | ***P* value** | **Baseline** | **Post** | ***P* value** |
| Peanut | 0.83 (<0.07-32.8) | 11.3 (0.57-291) | **<.001** | 0.59 (0.09-9.64) | 0.71 (0.09-5.12) | .22 |
| Ara h 1 | 0.07 (<0.07-0.92) | 1.28 (<0.07-16.6) | **<.001** | 0.07 (<0.07-4.14) | 0.07 (<0.07-1.74) | .12 |
| Ara h 2 | 0.13 (<0.07-3.72) | 4.73 (<0.07-250) | **<.001** | 0.19 (<0.07-1.00) | 0.11 (<0.07-0.98) | .21 |
| Ara h 3 | 0.07 (<0.07-7.03) | 0.34 (<0.07-21.3) | **<.001** | 0.07 (<0.07-6.94) | 0.07 (<0.07-2.19) | **.03** |
| Ara h 6* | 0.09 (<0.07-1.91) | 9.11 (<0.07-134) | **<.001** | 0.14 (<0.07-1.35) | 0.15 (<0.07-1.94) | .84 |
| Ara h 8 | 0.07 (<0.07-2.55) | 0.18 (<0.07-6.32) | **.006** | 0.07 (<0.07-1.51) | 0.07 (<0.07-0.35) | .37 |
| Ara h 9 | 0.09 (<0.07-14.1) | 0.13 (<0.07-70.1) | .12 | 0.07 (<0.07-2.35) | 0.07 (<0.07-2.32) | .67 |

Boldface *P* values are statistically significant.
Values are presented in mg/L as median (range).
*n = 38 and 19.